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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	10	MAR 22	PATDPASPC - New patent database available
NEWS	11	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	12	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	13	APR 04	EMBASE - Database reloaded and enhanced
NEWS	14	APR 18	New CAS Information Use Policies available online
NEWS	15	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	17	MAY 23	GBFULL enhanced with patent drawing images
NEWS	18	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	19	JUN 06	STN Patent Forums to be held in June 2005
NEWS	20	JUN 06	The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available
NEWS	21	JUN 13	RUSSIAPAT: New full-text patent database on STN
NEWS	22	JUN 13	FRFULL enhanced with patent drawing images
NEWS	23	JUN 20	MEDICONF to be removed from STN

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

*PROMT - PROMT from 1978 - present

* The files listed above are temporarily unavailable.

FILE 'HOME' ENTERED AT 12:12:28 ON 22 JUN 2005

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:12:36 ON 22 JUN 2005
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 JUN 2005 HIGHEST RN 852656-52-1
DICTIONARY FILE UPDATES: 21 JUN 2005 HIGHEST RN 852656-52-1

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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+                                                                   +
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
+                                                                   +
+++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++++
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end

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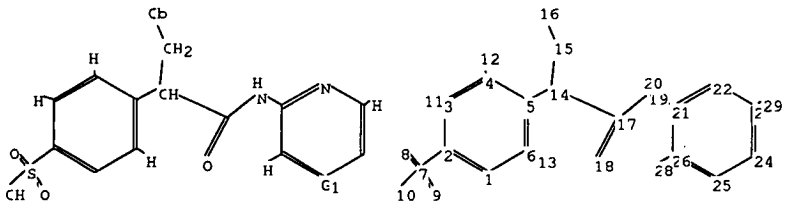
Uploading C:\Program Files\Stnexp\Queries\DIABETIC SULFONYLS 10732838.str

STN SEARCH TRANSCRIPT
10/732,838



chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 20 28 29
ring nodes :
1 2 3 4 5 6 21 22 23 24 25 26
chain bonds :
2-7 3-11 4-12 5-14 6-13 7-8 7-9 7-10 14-15 14-17 15-16 17-18 17-19
19-20 19-21 23-29 26-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
2-7 3-11 4-12 5-14 6-13 7-8 7-9 7-10 14-15 14-17 15-16 17-18 17-19
19-20 19-21 21-22 21-26 22-23 23-24 23-29 24-25 25-26 26-28
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:C,N

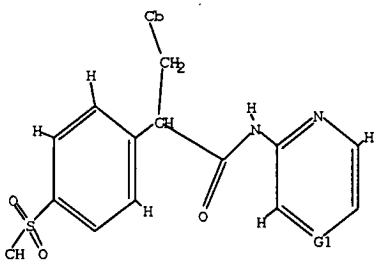
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 28:CLASS
29:CLASS
Generic attributes :
16:
Saturation : Saturated

L1 STRUCTURE UPLOADED

=> que L1

L2 QUE L1

=> D L2
L2 HAS NO ANSWERS
L1 STR



G1 C,N

Structure attributes must be viewed using STN Express query preparation.
L2 QUE ABB=ON PLU=ON L1

=> S L2
SAMPLE SEARCH INITIATED 12:13:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

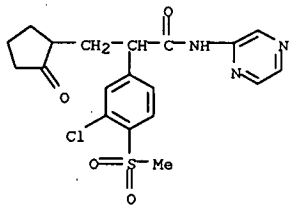
100.0% PROCESSED 12 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 33 TO 447
PROJECTED ANSWERS: 7 TO 298

L3 7 SEA SSS SAM L1

=> D 7

L3 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2005 ACS on STN
RN 625113-63-5 REGISTRY
ED Entered STN: 09 Dec 2003
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[(2-oxocyclopentyl)methyl]-N-pyrazinyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(2-oxocyclopentyl)-N-(pyrazin-2-yl)propionamide
FS 3D CONCORD
MF C19 H20 Cl N3 O4 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> S L2 SSS FULL
FULL SEARCH INITIATED 12:28:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    298 TO ITERATE

100.0% PROCESSED     298 ITERATIONS                          179 ANSWERS
SEARCH TIME: 00.00.01

L4          179 SEA SSS FUL L1

=> FILE CAPLUS
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             173.92     174.13

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FILE COVERS 1907 - 22 Jun 2005  VOL 142 ISS 26
FILE LAST UPDATED: 21 Jun 2005  (20050621/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> S L4
L5            5 L4

=> D 1-5
```

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:515493 CAPLUS
DN 141:71565
TI Preparation of pyrazines and related compounds as glucokinase activators for the treatment of type II diabetes
IN Chen, Shaoqing; Corbett, Wendy Lea; Guertin, Kevin Richard; Haynes, Nancy-Ellen; Kester, Robert Francis; Mennona, Francis A.; Mischke, Steven Gregory; Qian, Yimin; Sarabu, Ramakanth; Scott, Nathan Robert; Thakkar, Kshitij Chhabilbhai
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 243 pp.
CODEN: PIXXD2
DT Patent
LA English

APPLICANTS

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004052869	A1	20040624	WO 2003-EP14055	20031211
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004147748	A1	20040729	US 2003-732838	20031210
PRAI	US 2002-432806P	P	20021212		
	US 2003-524531P	P	20031124		
OS	MARPAT 141:71565				

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:913152 CAPLUS
DN 139:395954
TI Preparation of N-heteroaryl phenylacetamides and related compounds as glucokinase activators for treatment of type II diabetes
IN Corbett, Wendy Lea; Grimsby, Joseph Samuel; Haynes, Nancy-Ellen; Kester, Robert Francis; Mahaney, Paige Erin; Racha, Jagdish Kumar; Sarabu, Ramakanth; Wang, Ka
PA F. Hoffmann-La Roche AG, Switz.
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003095438	A1	20031120	WO 2003-EP3844	20030414
	WO 2003095438	C2	20041223		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	EP 1501815	A1	20050202	EP 2003-749855	20030414
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

	BR 2003009546	A	20050215	BR 2003-9546	20030414
	US 2003225283	A1	20031204	US 2003-421109	20030423
PRAI	US 2002-376161P	P	20020426		
	WO 2003-EP3844	W	20030414		

OS MARPAT 139:395954
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:667406 CAPLUS
DN 139:214460
TI Preparation of cycloalkylheteroaryl propionamides as glucokinase activators for treatment of type II diabetes
IN Bizzarro, Fred Thomas; Corbett, Wendy Lea; Grippo, Joseph Francis; Haynes, Nancy-Ellen; Holland, George William; Kester, Robert Francis; Mahaney, Paige Erin; Sarabu, Ramakanth
PA Hoffmann-La Roche Inc., USA
SO U.S., 92 pp., Cont.-in-part of U.S. 6,320,050.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6610846	B1	20030826	US 2000-675781	20000928
	US 2001039344	A1	20011108	US 2000-526143	20000315
	US 6320050	B2	20011120		
	ZA 2001007833	A	20021223	ZA 2001-7833	20010921
	US 2004014968	A1	20040122	US 2003-616359	20030709
PRAI	US 1999-126707P	P	19990329		
	US 1999-165944P	P	19991117		
	US 2000-526143	A2	20000315		
	US 2000-675781	A3	20000928		

OS MARPAT 139:214460
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:516858 CAPLUS
DN 139:65384
TI Methods for purification and crystal structure of human glucokinase and their use in treatment of type II diabetes
IN Corbett, Wendy Lea; Crowther, Robert Lewis; Dunten, Pete William; Kammlott, R. Ursula; Lukacs, Christine Maria
PA F. Hoffmann-La Roche AG, Switz.
SO Fr. Demande, 90 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2834295	A1	20030704	FR 2002-16171	20021219
	FR 2834295	B1	20050304		
	US 2003219887	A1	20031127	US 2002-318308	20021212
	GB 2385328	A1	20030820	GB 2002-29456	20021218
	DE 10259786	A1	20030717	DE 2002-10259786	20021219
	JP 2003235551	A2	20030826	JP 2002-367592	20021219
PRAI	US 2001-341988P	P	20011219		

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:707150 CAPLUS
DN 133:281775
TI Preparation of arylcycloalkylpropionamides as glucokinase activators.
IN Bizzarro, Fred Thomas; Corbett, Wendy Lea; Focella, Antonino; Grippo, Joseph Francis; Haynes, Nancy-ellen; Holland, George William; Kester, Robert Francis; Mahaney, Paige E.; Sarabu, Ramakanth
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 353 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000058293	A2	20001005	WO 2000-EP2450	20000320
	WO 2000058293	A3	20010125		
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2368347	AA	20001005	CA 2000-2368347	20000320
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	EP 1169312	A2	20020109	EP 2000-918816	20000320
	EP 1169312	B1	20041006		
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	TR 200102805	T2	20020422	TR 2001-200102805	20000320
	JP 2002540196	T2	20021126	JP 2000-607996	20000320
	AU 767830	B2	20031127	AU 2000-39630	20000320
	AU 2000039630	A5	20001016		
	NZ 514038	A	20040130	NZ 2000-514038	20000320
	AT 278680	E	20041015	AT 2000-918816	20000320
	RU 2242469	C2	20041220	RU 2001-126559	20000320
	ES 2226811	T3	20050401	ES 2000-918816	20000320
	US 6528543	B1	20030304	US 2000-532506	20000321
	HR 2001000688	A1	20030630	HR 2001-688	20010919
	ZA 2001007833	A	20021223	ZA 2001-7833	20010921
	NO 2001004671	A	20010926	NO 2001-4671	20010926
	HK 1046139	A1	20041210	HK 2002-107692	20021023
PRAI	US 1999-126707P	P	19990329		
	US 1999-165944P	P	19991117		
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	WO 2000-EP2450	W	20000320		

OS MARPAT 133:281775

=> D 2-5 IBIB ABS HITSTR

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:913152 CAPLUS
DOCUMENT NUMBER: 139:395954
TITLE: Preparation of N-heteroaryl phenylacetamides and related compounds as glucokinase activators for treatment of type II diabetes
INVENTOR(S): Corbett, Wendy Lea; Grimsby, Joseph Samuel; Haynes, Nancy-Ellen; Kester, Robert Francis; Mahaney, Paige Erin; Racha, Jagdish Kumar; Sarabu, Ramakanth; Wang, Ka
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095438	A1	20031120	WO 2003-EP3844	20030414
WO 2003095438	C2	20041223		
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EP 1501815	A1	20050202	EP 2003-749855	20030414
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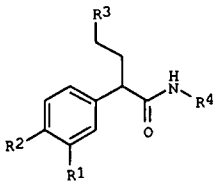
US 2003225283	A1	20031204	US 2003-421109	20030423
PRIORITY APPLN. INFO.:			US 2002-376161P P	20020426
			WO 2003-EP3844 W	20030414

OTHER SOURCE(S): MARPAT 139:395954
GI

THESE COMPOUNDS ARE IN 60/376,161



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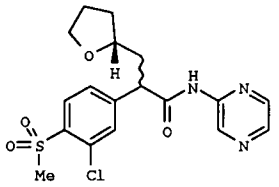


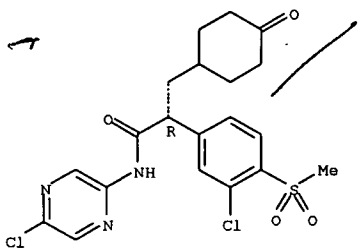
II

AB Title compds. I [wherein R1 and R2 = independently H, halo, (hydroxy)amino, CN, NO2, (perfluoro)alkyl, (perfluoro)alkylthio, (perfluoro)alkylsulfonyl, alkylsulfinyl, sulfonamido, OR5, or CO2R6; R3 = (un)substituted unbranched (hetero)alkyl; or CR3 = (hetero)cyclyl; R4 = CONHR6 or (un)substituted heteroaryl; R5 = H or (perfluoro)alkyl; R6 = alkyl; and pharmaceutically acceptable salts thereof] were prepared as glucokinase (GK) activators. For example, reaction of (3-chloro-4-methylsulfanylphenyl)acetic acid Me ester and trifluoromethanesulfonic acid ((R)-tetrahydrofuran-2-yl)methyl ester (preparation of starting materials given) produced 2-(3-chloro-4-methylsulfanylphenyl)-3-(tetrahydrofuran-2(R)-yl)propionic acid Me ester (52%), which was saponified with 0.8M aqueous LiOH to give the acid (95.8%). Amidation with 2-aminopyrazine (66.1%) in the presence of DMF and oxalyl chloride in CH2Cl2, followed by oxidation with 30% aqueous hydrogen peroxide afforded II (67.1%). SC1.5 (concentration producing a 50% increase in activity) values of ≤ 30 μM for activation of human liver GK1 expressed in E. coli as a glutathione S-transferase fusion protein (GST-GT) were obtained for all of the synthesized invention compds. Thus, I and their pharmaceutical compns. are useful in the treatment of type II diabetes (no data).

IT **625112-91-6I**, 2-(R)-[3-Chloro-4-(methanesulfonyl)phenyl]-N-(5-chloropyrazin-2-yl)-3-(4-oxocyclohexyl)propionamide **625113-40-8P** **625113-95-3I** **625114-26-3I**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(3-oxocyclopentyl)-N-(pyrazin-2-yl)propionamide **625114-44-5I**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-(3-oxocyclopentyl)propionamide **625114-55-8I**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(4-oxocyclohexyl)-N-(pyrazin-2-yl)propionamide **625114-61-6I**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-(4-oxocyclohexyl)propionamide **625114-62-7I** **625114-65-0P** **625114-67-2I** **625114-68-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(GK activator; preparation of phenylacetamides as glucokinase activators for treatment of type II diabetes)

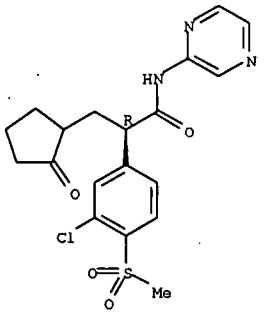
RN 625112-91-6 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloropyrazinyl)-4-(methylsulfonyl)-α-[(4-oxocyclohexyl)methyl]-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



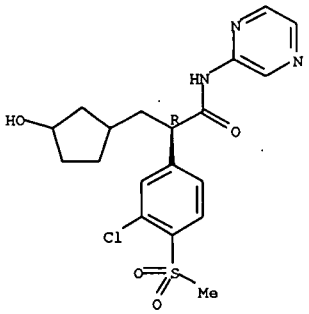
RN 625113-40-8 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[(2-oxocyclopentyl)methyl]-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

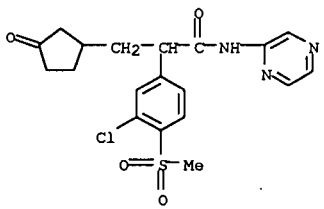


RN 625113-95-3 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[(3-hydroxycyclopentyl)methyl]-4-(methylsulfonyl)-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

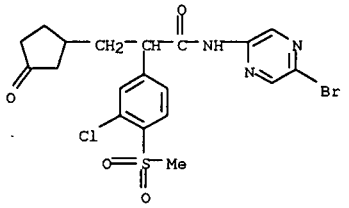


RN 625114-26-3 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[(3-oxocyclopentyl)methyl]-N-pyrazinyl- (9CI) (CA INDEX NAME)

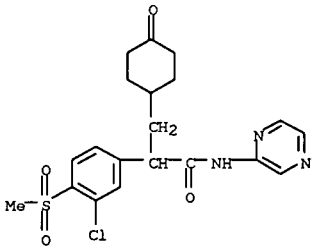


RN 625114-44-5 CAPLUS

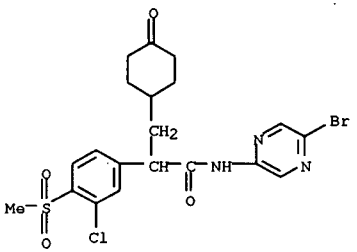
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-4-(methylsulfonyl)α-[(3-oxocyclopentyl)methyl]- (9CI) (CA INDEX NAME)



RN 625114-55-8 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[(4-oxocyclohexyl)methyl]-N-pyrazinyl- (9CI) (CA INDEX NAME)

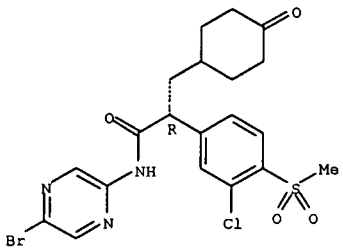


RN 625114-61-6 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-4-(methylsulfonyl)α-[(4-oxocyclohexyl)methyl]- (9CI) (CA INDEX NAME)



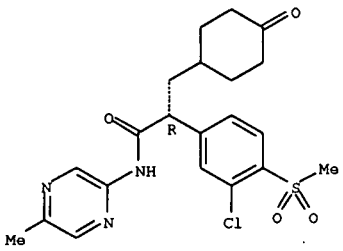
RN 625114-62-7 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-4-(methylsulfonyl)α-[(4-oxocyclohexyl)methyl]-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



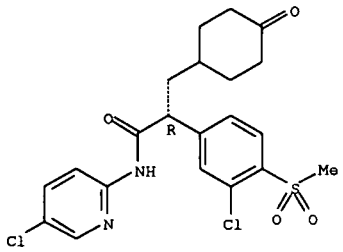
RN 625114-65-0 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-methylpyrazinyl)-4-(methylsulfonyl)-α-[(4-oxocyclohexyl)methyl]-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



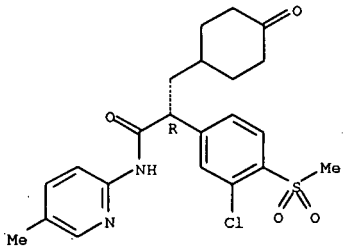
RN 625114-67-2 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloro-2-pyridinyl)-4-(methylsulfonyl)-α-[(4-oxocyclohexyl)methyl]-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 625114-68-3 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-methyl-2-pyridinyl)-4-(methylsulfonyl)-α-[(4-oxocyclohexyl)methyl]-, αR)- (9CI) (CA INDEX NAME)

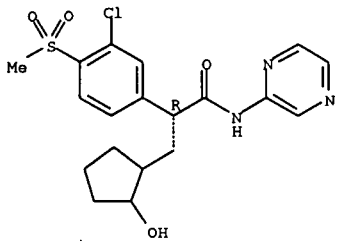
Absolute stereochemistry. Rotation (-).



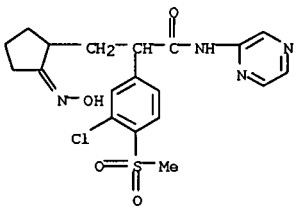
IT **625113-54-4P 625113-56-6P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(2-hydroxyiminocyclopentyl)-N-(pyrazin-2-yl)propionamide **625113-65-7P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-[2-(methoxyimino)cyclopentyl]-N-(pyrazin-2-yl)propionamide **625114-35-4P 625114-41-2P 625114-46-7P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(3-hydroxyiminocyclopentyl)-N-(pyrazin-2-yl)propionamide **625114-47-8P**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-(3-hydroxyiminocyclopentyl)propionamide **625114-49-0P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-[3-(methoxyimino)cyclopentyl]-N-(pyrazin-2-yl)propionamide **625114-50-3P**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-[3-(methoxyimino)cyclopentyl]propionamide **625114-54-7P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(3-hydroxy-3-methylcyclopentyl)-N-(pyrazin-2-yl)propionamide **625114-69-4P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(4-hydroxyiminocyclohexyl)-N-(pyrazin-2-yl)propionamide **625114-70-7P**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-(4-hydroxyiminocyclohexyl)propionamide **625114-71-8P 625114-72-9P 625114-73-0P 625114-74-1P 625114-75-2P 625114-76-3P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-[4-(methoxyimino)cyclohexyl]-N-(pyrazin-2-yl)propionamide **625114-77-4P**, N-(5-Bromopyrazin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-[4-(methoxyimino)cyclohexyl]propionamide **625826-90-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GK activator; preparation of phenylacetamides as glucokinase activators for treatment of type II diabetes)

RN 625113-54-4 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[(2-hydroxycyclopentyl)methyl]-4-(methylsulfonyl)-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

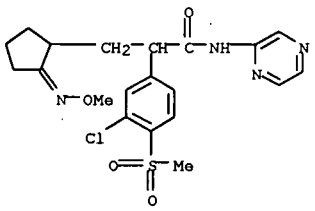
Absolute stereochemistry.



RN 625113-56-6 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[2-(hydroxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)

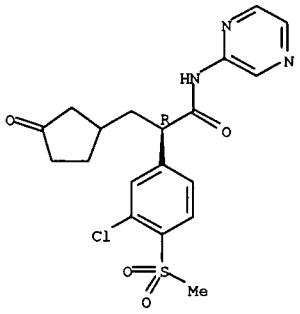


RN 625113-65-7 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[2-(methoxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



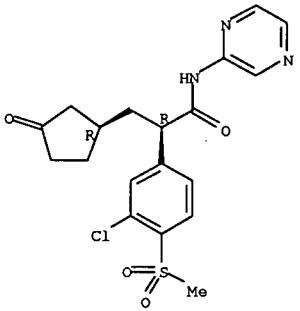
RN 625114-35-4 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[(3-oxocyclopentyl)methyl]-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

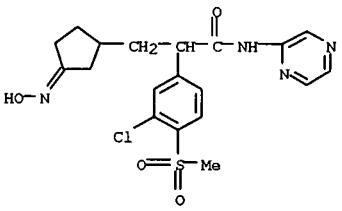


RN 625114-41-2 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)α-[[(1R)-3-oxocyclopentyl]methyl]-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

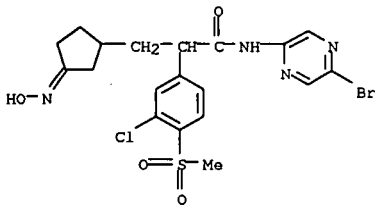


RN 625114-46-7 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[3-(hydroxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)

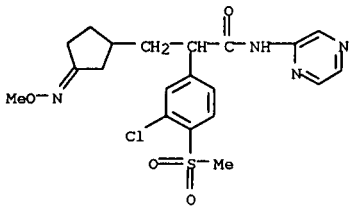


RN 625114-47-8 CAPLUS

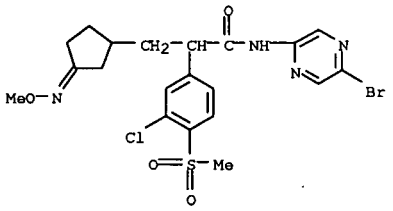
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-α-[[3-(hydroxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



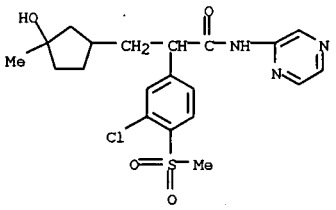
RN 625114-49-0 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[3-(methoxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



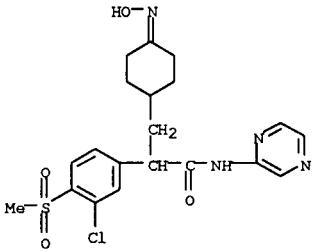
RN 625114-50-3 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-α-[[3-(methoxyimino)cyclopentyl]methyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



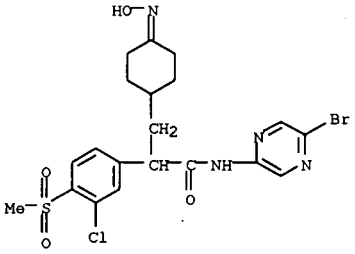
RN 625114-54-7 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[(3-hydroxy-3-methylcyclopentyl)methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



RN 625114-69-4 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[4-(hydroxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)

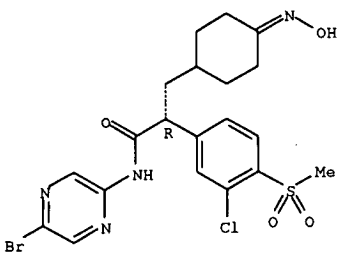


RN 625114-70-7 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-α-[[4-(hydroxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



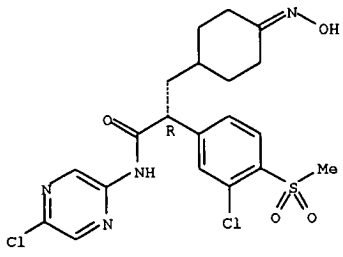
RN 625114-71-8 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-α-[[4-(hydroxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



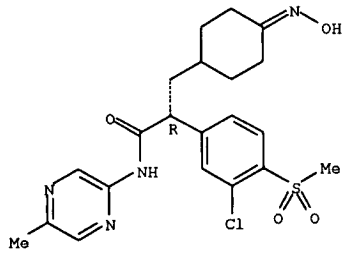
RN 625114-72-9 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloropyrazinyl)α-[[4-(hydroxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



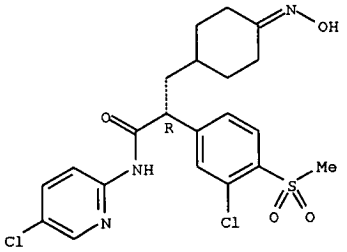
RN 625114-73-0 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[4-(hydroxyimino)cyclohexyl]methyl]-N-(5-methylpyrazinyl)-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



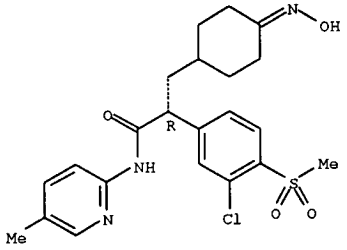
RN 625114-74-1 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloro-2-pyridinyl)α-[[4-(hydroxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

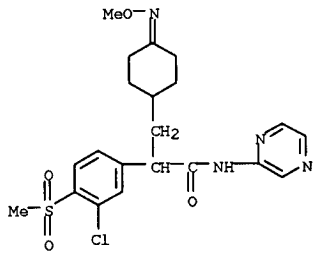


RN 625114-75-2 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[4-(hydroxyimino)cyclohexyl]methyl]-N-(5-methyl-2-pyridinyl)-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

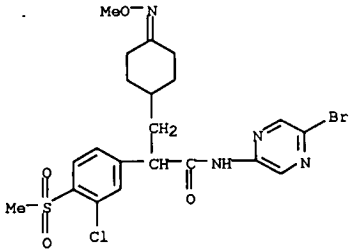
Absolute stereochemistry. Rotation (-).



RN 625114-76-3 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[4-(methoxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)

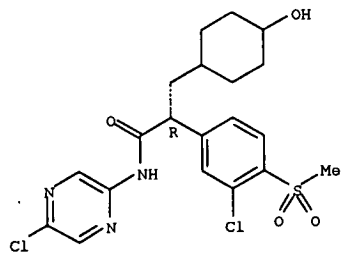


RN 625114-77-4 CAPLUS
CN Benzeneacetamide, N-(5-bromopyrazinyl)-3-chloro-α-[[4-(methoxyimino)cyclohexyl]methyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



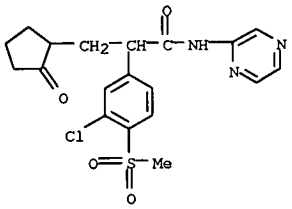
RN 625826-90-6 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloropyrazinyl)-α-[(4-hydroxycyclohexyl)methyl]-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



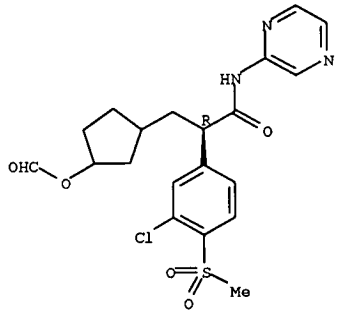
IT **625113-63-5P**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-(2-oxocyclopentyl)-N-(pyrazin-2-yl)propionamide**625114-02-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of phenylacetamides as glucokinase activators for treatment of type II diabetes)

RN 625113-63-5 CAPLUS
CN Benzeneacetamide, 3-chloro-4-(methylsulfonyl)-α-[(2-oxocyclopentyl)methyl]-N-pyrazinyl- (9CI) (CA INDEX NAME)



RN 625114-02-5 CAPLUS
CN Benzeneacetamide, 3-chloro-α-[[3-(formyloxy)cyclopentyl]methyl]-4-(methylsulfonyl)-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

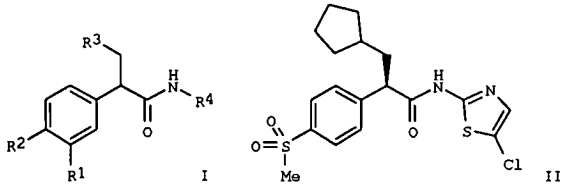
L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:667406 CAPLUS
DOCUMENT NUMBER: 139:214460
TITLE: Preparation of cycloalkylheteroaryl propionamides as glucokinase activators for treatment of type II diabetes
INVENTOR(S): Bizzarro, Fred Thomas; Corbett, Wendy Lea; Grippo, Joseph Francis; Haynes, Nancy-Ellen; Holland, George William; Kester, Robert Francis; Mahaney, Paige Erin; Sarabu, Ramakanth
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., USA
SOURCE: U.S., 92 pp., Cont.-in-part of U.S. 6,320,050.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6610846	B1	20030826	US 2000-675781	20000928
US 2001039344	A1	20011108	US 2000-526143	20000315

US 6320050	B2	20011120			
ZA 2001007833	A	20021223	ZA 2001-7833		20010921
US 2004014968	A1	20040122	US 2003-616359		20030709
PRIORITY APPLN. INFO.:			US 1999-126707P	P	19990329
			US 1999-165944P	P	19991117
			US 2000-526143	A2	20000315
			US 2000-675781	A3	20000928

OTHER SOURCE(S): MARPAT 139:214460

GI



I

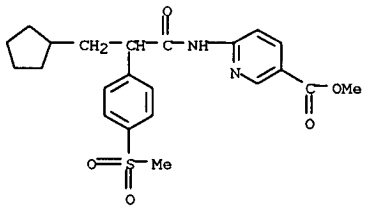
II

AB Title compds. [I; R1, R2 = H, halo, amino, hydroxyamino, NO2, cyano, sulfonamido, perfluoroalkyl, alkylthio, alkylsulfonyl, alkylsulfinyl, etc.; R3 = alkyl, cycloalkyl; R4 = certain un- or monosubstituted 5- and 6-membered heteroarom. rings connected by a ring C atom; R4 (claims) = un- or monosubstituted triazine, pyrazine, or pyridazine; and their pharmaceutical acceptable salts], were prepared via amidation, for use as glucokinase activators for treatment of type II diabetes. Thus, the invention compound N-(5-chlorothiazol-2-yl)-3-cyclopentyl-2(R)-[4-(methanesulfonyl)phenyl]propionamide (II) was prepared by addition of 3-cyclopentyl-2(R)-[4-(methanesulfonyl)phenyl]propionic acid (preparation given) to a stirred mixture of triphenylphosphine and N-bromosuccinimide in methylene chloride at 0°, followed by stirring at room temperature for 30 min, addition of a solution of 2-amino-5-chlorothiazole hydrochloride and pyridine in methylene chloride, and stirring at 25° overnight. All of the exemplified compds. I activated glucokinase in vitro, exhibiting an SC1.5 ≤ 30 μM. Selected invention compds. exhibited glucokinase activator activity in vivo when administered orally to mice. Thus, I are expected to increase insulin secretion in the treatment of type II diabetes.

IT **300355-49-1**, 6-[[3-Cyclopentyl-2-[4-(methanesulfonyl)phenyl]propionyl]amino]nicotinic acid methyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(glucokinase activator; preparation of cycloalkylheteroaryl propionamides as glucokinase activators)

RN 300355-49-1 CAPLUS

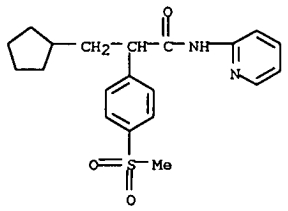
CN 3-Pyridinecarboxylic acid, 6-[[3-cyclopentyl-2-[4-(methylsulfonyl)phenyl]-1-oxopropyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



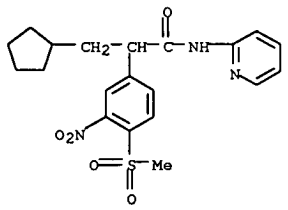
IT **300353-47-3**, 3-Cyclopentyl-2-[4-(methanesulfonyl)phenyl]-N-pyridin-2-ylpropionamide **300353-49-5**, 3-Cyclopentyl-2-[4-(methanesulfonyl)-3-nitrophenyl]-N-pyridin-2-ylpropionamide **300353-53-1**, 6-[[3-Cyclopentyl-2-[4-(methanesulfonyl)phenyl]propionyl]amino]nicotinic acid **300353-57-5**, 3-Cyclopentyl-N-(5-hydroxymethylpyridin-2-yl)-2-[4-(methanesulfonyl)phenyl]propionamide **300353-58-6**, 3-Cyclopentyl-2-[4-(methanesulfonyl)phenyl]-N-(5-methylpyridin-2-yl)propionamide **300353-75-7**, N-(5-Bromopyridin-2-yl)-3-cyclopentyl-2-[4-(methanesulfonyl)-3-nitrophenyl]propionamide **300353-82-6**, 2-[3-Bromo-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyridin-2-ylpropionamide **300353-83-7**, 2-[3-Bromo-4-(methanesulfonyl)phenyl]-N-(5-bromopyridin-2-yl)-3-cyclopentylpropionamide **300353-85-9**, 2-[3-Cyano-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyridin-2-ylpropionamide **300353-87-1**, 3-Cyclopentyl-2-[4-(ethanesulfonyl)phenyl]-N-pyridin-2-ylpropionamide **300353-89-3**, 2-[3,4-Bis(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyridin-2-ylpropionamide **300354-03-4**, 3-Cyclopentyl-2-[4-(methanesulfonyl)-3-trifluoromethylphenyl]-N-pyridin-2-ylpropionamide **300354-05-6**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyridin-2-ylpropionamide **300354-06-7**, N-(5-Bromopyridin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-cyclopentylpropionamide **300354-07-8**, N-(5-Chloropyridin-2-yl)-2-[3-chloro-4-(methanesulfonyl)phenyl]-3-cyclopentylpropionamide **300354-08-9**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-(5-trifluoromethylpyridin-2-yl)propionamide **300354-11-4**, 2(R)-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyridin-2-ylpropionamide **300354-12-5**, N-(5-Bromopyridin-2-yl)-2(R)-[3-chloro-4-(methanesulfonyl)phenyl]-3-cyclopentylpropionamide **588939-59-7**, 3-Cyclopentyl-2(R)-(4-methylsulfonylphenyl)-N-pyrazin-2-ylpropionamide **588940-56-1**, 3-Cyclopentyl-2-[3-fluoro-4-(methanesulfonyl)phenyl]-N-pyridin-2-ylpropionamide **588940-95-8P**, 2(R)-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-(5-methylpyridin-2-yl)propionamide **588941-40-6**, 2-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyrazin-2-ylpropionamide **588941-45-1**, 2(R)-[3-Chloro-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyrazin-2-ylpropionamide **588941-62-2**, 2-[3-Bromo-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyrazin-2-ylpropionamide **588941-84-8**, 2-[3-Cyano-4-(methanesulfonyl)phenyl]-3-cyclopentyl-N-pyrazin-2-ylpropionamide **588942-11-4**, 3-Cyclopentyl-2-[4-(methanesulfonyl)-3-trifluoromethylphenyl]-N-pyrazin-2-ylpropionamide **588942-19-2**, N-(5-Bromopyridin-2-yl)-3-cyclopentyl-2-[4-(methanesulfonyl)-3-trifluoromethylphenyl]propionamide **588942-55-6**, 3-Cyclopentyl-2(R)-[4-(methanesulfonyl)-3-trifluoromethylphenyl]-N-pyrazin-2-ylpropionamide **588942-76-1**, 3-Cyclopentyl-2-[4-(methanesulfonyl)-3-nitrophenyl]-N-pyrazin-2-ylpropionamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(glucokinase activator; preparation of cycloalkylheteroaryl propionamides as glucokinase activators)

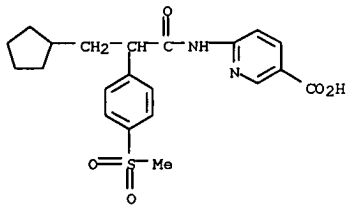
RN 300353-47-3 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



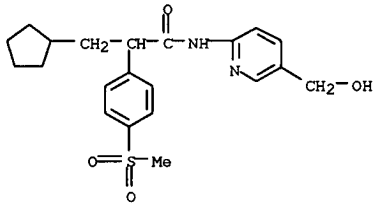
RN 300353-49-5 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-nitro-N-2-pyridinyl- (9CI) (CA INDEX NAME)



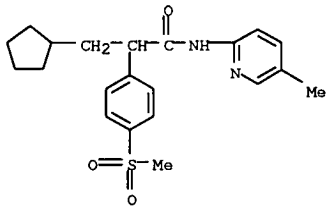
RN 300353-53-1 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[[3-cyclopentyl-2-[4-(methylsulfonyl)phenyl]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



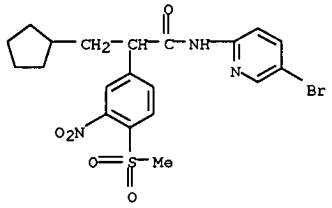
RN 300353-57-5 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-N-[5-(hydroxymethyl)-2-pyridinyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



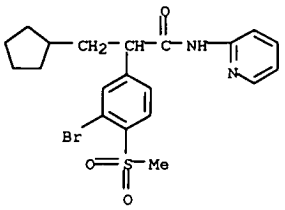
RN 300353-58-6 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-N-(5-methyl-2-pyridinyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



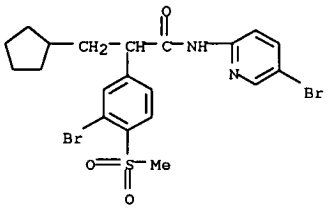
RN 300353-75-7 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-nitro- (9CI) (CA INDEX NAME)



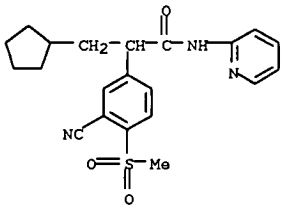
RN 300353-82-6 CAPLUS
CN Benzeneacetamide, 3-bromo-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



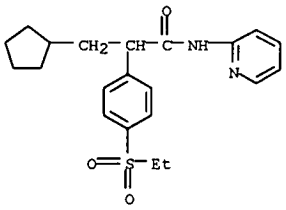
RN 300353-83-7 CAPLUS
CN Benzeneacetamide, 3-bromo-N-(5-bromo-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



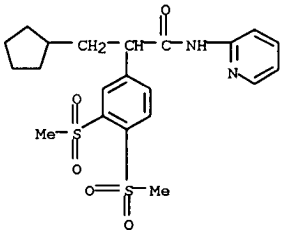
RN 300353-85-9 CAPLUS
CN Benzeneacetamide, 3-cyano-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



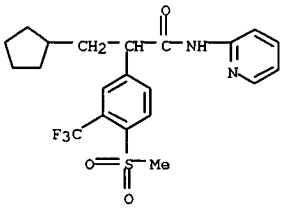
RN 300353-87-1 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(ethylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



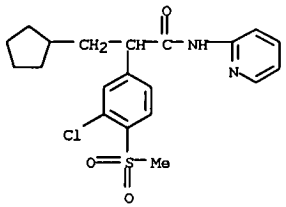
RN 300353-89-3 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-3,4-bis(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



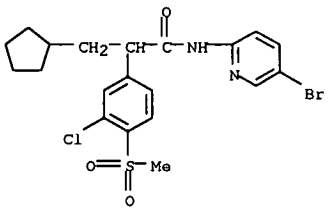
RN 300354-03-4 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



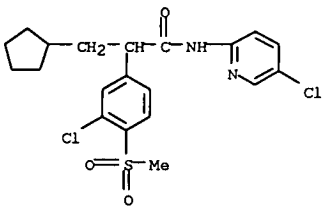
RN 300354-05-6 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



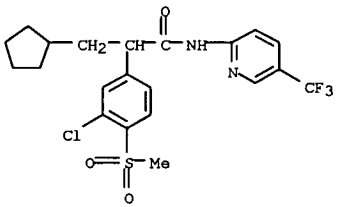
RN 300354-06-7 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)-3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



RN 300354-07-8 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloro-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

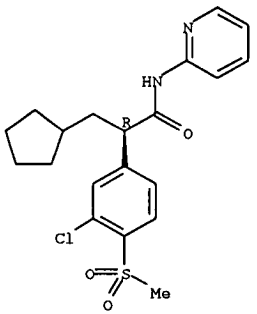


RN 300354-08-9 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-[5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



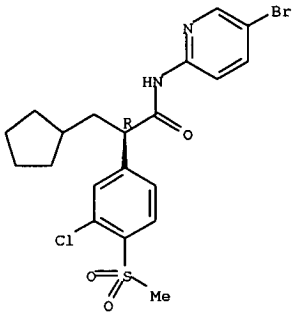
RN 300354-11-4 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



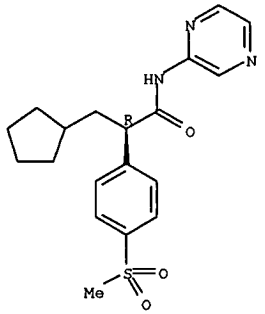
RN 300354-12-5 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)-3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

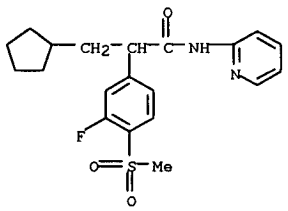


RN 588939-59-7 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

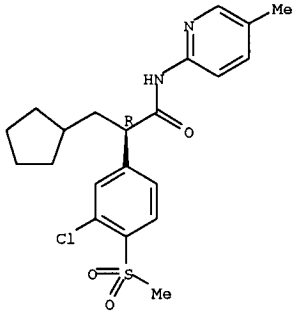


RN 588940-56-1 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-3-fluoro-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)

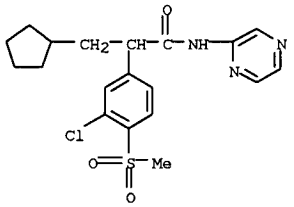


RN 588940-95-8 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-N-(5-methyl-2-pyridinyl)-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

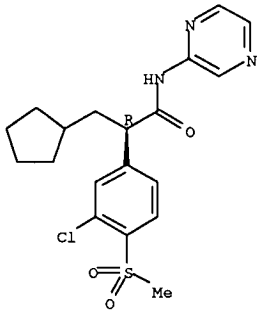


RN 588941-40-6 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



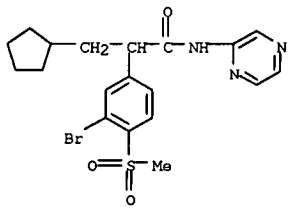
RN 588941-45-1 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

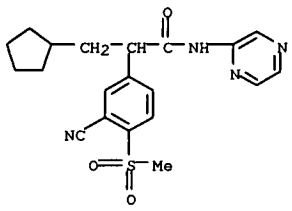


RN 588941-62-2 CAPLUS

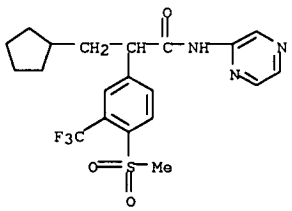
CN Benzeneacetamide, 3-bromo-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



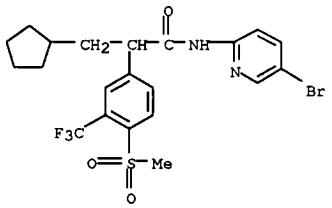
RN 588941-84-8 CAPLUS
CN Benzeneacetamide, 3-cyano-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl- (9CI) (CA INDEX NAME)



RN 588942-11-4 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

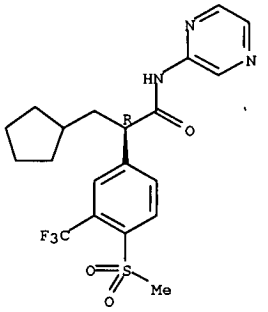


RN 588942-19-2 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

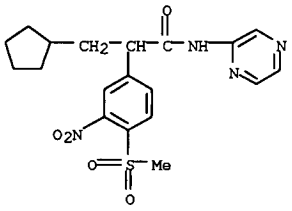


RN 588942-55-6 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-pyrazinyl-3-(trifluoromethyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 588942-76-1 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-nitro-N-pyrazinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:516858 CAPLUS
DOCUMENT NUMBER: 139:65384
TITLE: Methods for purification and crystal structure of

human glucokinase and their use in treatment of type II diabetes

INVENTOR(S): Corbett, Wendy Lea; Crowther, Robert Lewis; Dunten, Pete William; Kammlott, R. Ursula; Lukacs, Christine Maria

PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.

SOURCE: Fr. Demande, 90 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2834295	A1	20030704	FR 2002-16171	20021219
FR 2834295	B1	20050304		
US 2003219887	A1	20031127	US 2002-318308	20021212
GB 2385328	A1	20030820	GB 2002-29456	20021218
DE 10259786	A1	20030717	DE 2002-10259786	20021219
JP 2003235551	A2	20030826	JP 2002-367592	20021219

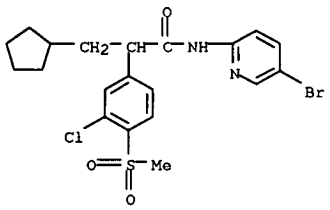
PRIORITY APPLN. INFO.: US 2001-341988P P 20011219

AB This invention relates to crystal structure of human glucokinase and methods for culturing these proteins. Methods of using glucokinase for treatment of hyperglycemia in type II diabetes are provided.

IT **300354-06-7 300354-08-9**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cocrystn. of glucokinase with; methods for purification and crystal structure of human glucokinase and their use in treatment of type II diabetes)

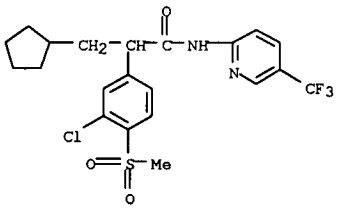
RN 300354-06-7 CAPLUS

CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)-3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



RN 300354-08-9 CAPLUS

CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-[5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:707150 CAPLUS

DOCUMENT NUMBER: 133:281775

TITLE: Preparation of arylcycloalkylpropionamides as glucokinase activators.

INVENTOR(S): Bizzarro, Fred Thomas; Corbett, Wendy Lea; Focella, Antonino; Grippo, Joseph Francis; Haynes, Nancy-ellen; Holland, George William; Kester, Robert Francis; Mahaney, Paige E.; Sarabu, Ramakanth

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 353 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

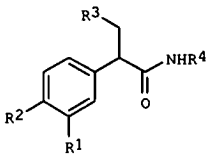
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058293	A2	20001005	WO 2000-EP2450	20000320
WO 2000058293	A3	20010125		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368347	AA	20001005	CA 2000-2368347	20000320
BR 2000009486	A	20020102	BR 2000-9486	20000320
EP 1169312	A2	20020109	EP 2000-918816	20000320
EP 1169312	B1	20041006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102805	T2	20020422	TR 2001-200102805	20000320
JP 2002540196	T2	20021126	JP 2000-607996	20000320
AU 767830	B2	20031127	AU 2000-39630	20000320
AU 2000039630	A5	20001016		
NZ 514038	A	20040130	NZ 2000-514038	20000320
AT 278680	E	20041015	AT 2000-918816	20000320
RU 2242469	C2	20041220	RU 2001-126559	20000320
ES 2226811	T3	20050401	ES 2000-918816	20000320
US 6528543	B1	20030304	US 2000-532506	20000321
HR 2001000688	A1	20030630	HR 2001-688	20010919
ZA 2001007833	A	20021223	ZA 2001-7833	20010921
NO 2001004671	A	20010926	NO 2001-4671	20010926
HK 1046139	A1	20041210	HK 2002-107692	20021023

PRIORITY APPLN. INFO.: US 1999-126707P P 19990329
US 1999-165944P P 19991117
US 1999-165948P P 19991117
WO 2000-EP2450 W 20000320

OTHER SOURCE(S): MARPAT 133:281775

GI

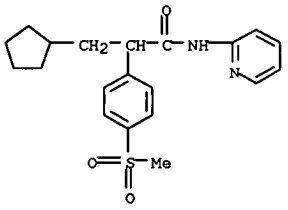


I

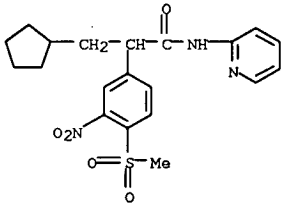
AB Title compds. [I; R1, R2 = H, halo, amino, hydroxyamino, NO2, cyano, sulfonamido, perfluoroalkyl, alkylthio, alkylsulfonyl, alkylsulfinyl, etc.; R3 = alkyl, cycloalkyl; R4 = CONHR40, (substituted) 5-6 membered heteroaryl; R40 = H, alkyl, alkenyl, hydroxyalkyl, haloalkyl, etc.], were prepared for treatment of type II diabetes. Thus, 3-cyclopentyl-2-(3,4-dichlorophenyl)propionic acid (preparation given), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate, and 2-aminothiazole in CH2Cl2 was treated with Et3N followed by 14 h stirring to give 3-cyclopentyl-2-(3,4-dichlorophenyl)-N-thiazol-2-ylpropionamide. I activated glucokinase in vitro with SC1.≤30 μM.

IT **300353-47-3I 300353-49-5I 300353-53-1P**
300353-57-5I 300353-58-6I 300353-75-7P
300353-82-6I 300353-83-7I 300353-85-9P
300353-87-1I 300353-89-3I 300354-03-4P
300354-05-6I 300354-06-7I 300354-07-8P
300354-08-9I 300354-11-4I 300354-12-5P
300355-49-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylcycloalkylpropionamides as glucokinase activators)

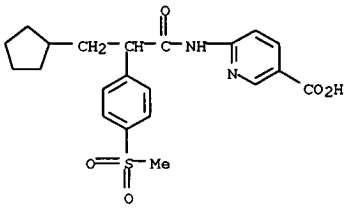
RN 300353-47-3 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



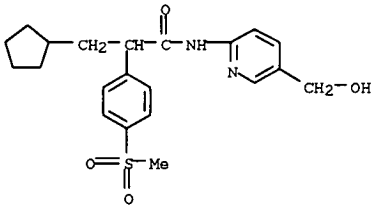
RN 300353-49-5 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-nitro-N-2-pyridinyl- (9CI) (CA INDEX NAME)



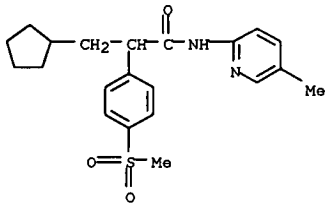
RN 300353-53-1 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[[3-cyclopentyl-2-[4-(methylsulfonyl)phenyl]-1-oxopropyl]amino]- (9CI) (CA INDEX NAME)



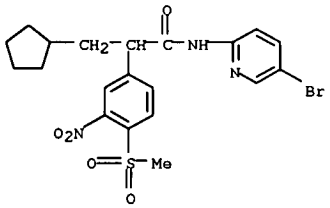
RN 300353-57-5 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-N-[5-(hydroxymethyl)-2-pyridinyl]-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



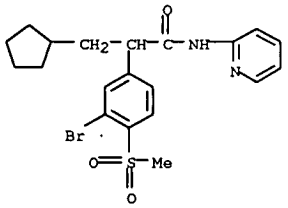
RN 300353-58-6 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-N-(5-methyl-2-pyridinyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



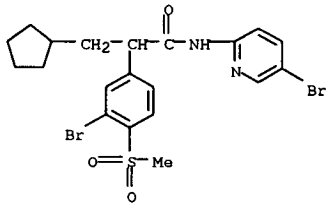
RN 300353-75-7 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)-3-nitro- (9CI) (CA INDEX NAME)



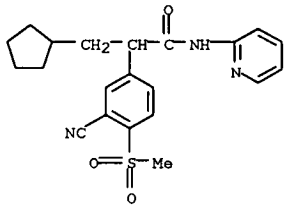
RN 300353-82-6 CAPLUS
CN Benzeneacetamide, 3-bromo-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



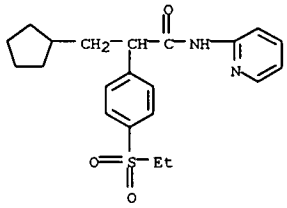
RN 300353-83-7 CAPLUS
CN Benzeneacetamide, 3-bromo-N-(5-bromo-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



RN 300353-85-9 CAPLUS
CN Benzeneacetamide, 3-cyano-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



RN 300353-87-1 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(ethylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



RN 300353-89-3 CAPLUS
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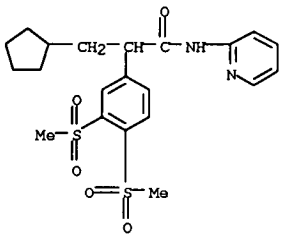
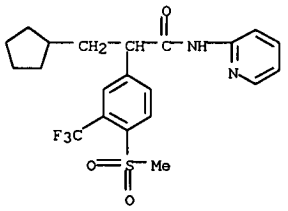
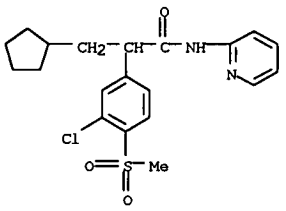


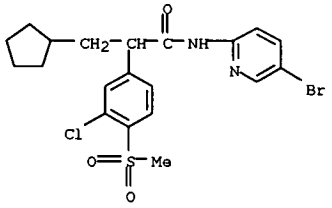
RN 300354-03-4 CAPLUS
CN Benzeneacetamide, α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



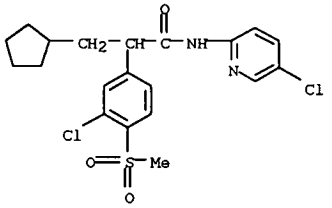
RN 300354-05-6 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl- (9CI) (CA INDEX NAME)



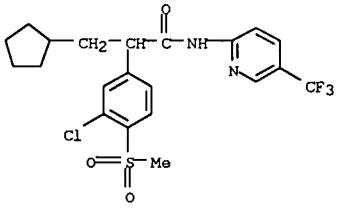
RN 300354-06-7 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)-3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)



RN 300354-07-8 CAPLUS
CN Benzeneacetamide, 3-chloro-N-(5-chloro-2-pyridinyl)α-(cyclopentylmethyl)-4-(methylsulfonyl)- (9CI) (CA INDEX NAME)

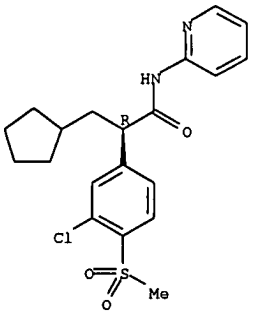


RN 300354-08-9 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-[5-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



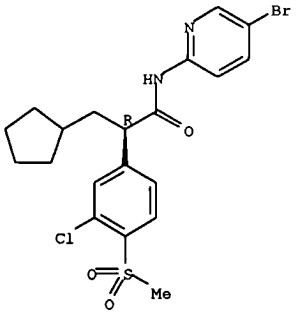
RN 300354-11-4 CAPLUS
CN Benzeneacetamide, 3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-N-2-pyridinyl-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

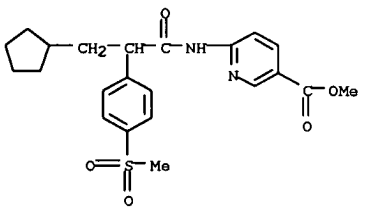


RN 300354-12-5 CAPLUS
CN Benzeneacetamide, N-(5-bromo-2-pyridinyl)-3-chloro-α-(cyclopentylmethyl)-4-(methylsulfonyl)-, αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 300355-49-1 CAPLUS
CN 3-Pyridinecarboxylic acid, 6-[[3-cyclopentyl-2-[4-(methylsulfonyl)phenyl]-1-oxopropyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



=> LOG HOLD

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	26.61	200.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.92	-2.92

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 12:29:44 ON 22 JUN 2005

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                   data from INPADOC
 NEWS  4  FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  5  MAR 02   GBFULL: New full-text patent database on STN
 NEWS  6  MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  7  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  9  MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
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 NEWS  11 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  12 APR 04   EPFULL enhanced with additional patent information and new
                   fields
 NEWS  13 APR 04   EMBASE - Database reloaded and enhanced
 NEWS  14 APR 18   New CAS Information Use Policies available online
 NEWS  15 APR 25   Patent searching, including current-awareness alerts (SDIs),
                   based on application date in CA/CAplus and USPATFULL/USPAT2
                   may be affected by a change in filing date for U.S.
                   applications.
 NEWS  16 APR 28   Improved searching of U.S. Patent Classifications for
                   U.S. patent records in CA/CAplus
 NEWS  17 MAY 23   GBFULL enhanced with patent drawing images
 NEWS  18 MAY 23   REGISTRY has been enhanced with source information from
                   CHEMCATS
 NEWS  19 JUN 06   STN Patent Forums to be held in June 2005
 NEWS  20 JUN 06   The Analysis Edition of STN Express with Discover!
                   (Version 8.0 for Windows) now available
 NEWS  21 JUN 13   RUSSIAPAT: New full-text patent database on STN
 NEWS  22 JUN 13   FRFULL enhanced with patent drawing images
 NEWS  23 JUN 20   MEDICONF to be removed from STN

 NEWS EXPRESS  JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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  of commercial gateways or other similar uses is prohibited and may
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FILE 'HOME' ENTERED AT 13:30:01 ON 22 JUN 2005

=> FILE MEDLINE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 13:30:12 ON 22 JUN 2005
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MEDLINE SEARCH FOR CL. 94

FILE LAST UPDATED: 21 JUN 2005 (20050621/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> S GLUCOKINASE ACTIVATORS
          2481 GLUCOKINASE
            31 GLUCOKINASES
          2483 GLUCOKINASE
                 (GLUCOKINASE OR GLUCOKINASES)
         47366 ACTIVATORS
L1           8 GLUCOKINASE ACTIVATORS
                 (GLUCOKINASE(W)ACTIVATORS)

=> S GLUCOKINASE ACTIVATOR
          2481 GLUCOKINASE
            31 GLUCOKINASES
          2483 GLUCOKINASE
                 (GLUCOKINASE OR GLUCOKINASES)
         62765 ACTIVATOR
         47366 ACTIVATORS
         97413 ACTIVATOR
                 (ACTIVATOR OR ACTIVATORS)
L2           9 GLUCOKINASE ACTIVATOR
                 (GLUCOKINASE(W)ACTIVATOR)

=> D 1-9

L2   ANSWER 1 OF 9     MEDLINE on STN
AN   2005175621     IN-PROCESS
DN   PubMed ID: 15808477
TI   Discovery, synthesis and biological evaluation of novel
     glucokinase activators.
AU   McKerrecher Darren; Allen Joanne V; Bowker Suzanne S; Boyd Scott; Caulkett
     Peter W R; Currie Gordon S; Davies Christopher D; Fenwick Mark L; Gaskin
     Harold; Grange Emma; Hargreaves Rod B; Hayter Barry R; James Roger;
     Johnson Keith M; Johnstone Craig; Jones Clifford D; Lackie Sarah; Rayner
     John W; Walker Rolf P
CS   Cardiovascular and Gastrointestinal Research Area, AstraZeneca UK,
     Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG, UK.
     darren.mckerrecher@astrazeneca.com. <darren.mckerrecher@astrazeneca.com>
SO   Bioorganic & medicinal chemistry letters, (2005 Apr 15) 15 (8) 2103-6.
     Journal code: 9107377. ISSN: 0960-894X.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED   Entered STN: 20050406
     Last Updated on STN: 20050426
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L2 ANSWER 2 OF 9 MEDLINE on STN
AN 2005154707 IN-PROCESS
DN PubMed ID: 15787609
TI Small molecule **glucokinase activators** as novel anti-diabetic agents.
AU Leighton B; Atkinson A; Coghlan M P
CS AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10 4TG, UK.. Brendan.Leighton@astrazeneca.com
SO Biochemical Society transactions, (2005 Apr) 33 (Pt 2) 371-4. Journal code: 7506897. ISSN: 0300-5127.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20050325
Last Updated on STN: 20050510

L2 ANSWER 3 OF 9 MEDLINE on STN
AN 2005083678 IN-PROCESS
DN PubMed ID: 15713416
TI Glucokinase-activating ureas.
AU Castelhano Arlindo L; Dong Hanqing; Fyfe Matthew C T; Gardner Lisa S; Kamikozawa Yukari; Kurabayashi Satomi; Nawano Masao; Ohashi Rikiya; Procter Martin J; Qiu Li; Rasamison Chrystelle M; Schofield Karen L; Shah Vilas K; Ueta Kiichiro; Williams Geoffrey M; Witter David; Yasuda Kosuke
CS OSI Pharmaceuticals, 1 Bioscience Park Drive, Farmingdale, NY 11735, USA.
SO Bioorganic & medicinal chemistry letters, (2005 Mar 1) 15 (5) 1501-4. Journal code: 9107377. ISSN: 0960-894X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20050217
Last Updated on STN: 20050316

L2 ANSWER 4 OF 9 MEDLINE on STN
AN 2004372863 MEDLINE
DN PubMed ID: 15277384
TI Insulin dose-response curves for stimulation of splanchnic glucose uptake and suppression of endogenous glucose production differ in nondiabetic humans and are abnormal in people with type 2 diabetes.
AU Basu Rita; Basu Ananda; Johnson C Michael; Schwenk W Frederick; Rizza Robert A
CS Division of Endocrinology, Mayo Clinic, Rochester, Minnesota 55905, USA.
NC DK29953 (NIDDK)
RR-00585 (NCRR)
SO Diabetes, (2004 Aug) 53 (8) 2042-50. Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200409
ED Entered STN: 20040728
Last Updated on STN: 20040921
Entered Medline: 20040917

L2 ANSWER 5 OF 9 MEDLINE on STN
AN 2004132273 MEDLINE
DN PubMed ID: 14988235
TI Stimulation of hepatocyte glucose metabolism by novel small molecule **glucokinase activators.**

AU Brocklehurst Katy J; Payne Victoria A; Davies Rick A; Carroll Debra; Vertigan Helen L; Wightman Heather J; Aiston Susan; Waddell Ian D; Leighton Brendan; Coghlan Matthew P; Agius Loranne
CS Cardiovascular and Gastrointestinal Department, AstraZeneca, Macclesfield, Cheshire, U.K.
SO Diabetes, (2004 Mar) 53 (3) 535-41.
Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200406
ED Entered STN: 20040318
Last Updated on STN: 20040609
Entered Medline: 20040608

L2 ANSWER 6 OF 9 MEDLINE on STN
AN 2004103919 MEDLINE
DN PubMed ID: 14993457
TI Two birds with one stone: novel **glucokinase activator** stimulates glucose-induced pancreatic insulin secretion and augments hepatic glucose metabolism.
AU Al-Hasani Hadi; Tschop Matthias H; Cushman Samuel W
CS Department of Pharmacology, German Institute of Human Nutrition, 14558 Potsdam-Rehbrucke, Germany.
SO Mol Interv, (2003 Oct) 3 (7) 367-70. Ref: 18
Journal code: 101093789. ISSN: 1534-0384.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040303
Last Updated on STN: 20040424
Entered Medline: 20040423

L2 ANSWER 7 OF 9 MEDLINE on STN
AN 2003458066 MEDLINE
DN PubMed ID: 14519091
TI Metabolic diseases drug discovery world summit. July 28-29, 2003, San Diego, CA, USA.
AU Sarabu Ramkanth
CS Hoffmann-La Roche, Inc. 340 Kingsland Street, Nutley, NJ 07110, USA.. ramakanth.sarabu@roche.com
SO Expert opinion on investigational drugs, (2003 Oct) 12 (10) 1721-6.
Journal code: 9434197. ISSN: 1354-3784.
CY England: United Kingdom
DT Conference; Conference Article; (CONGRESSES)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20031002
Last Updated on STN: 20040312
Entered Medline: 20040311

L2 ANSWER 8 OF 9 MEDLINE on STN
AN 1999408474 MEDLINE
DN PubMed ID: 10480597
TI Structural model of human glucokinase in complex with glucose and ATP: implications for the mutants that cause hypo- and hyperglycemia.
AU Mahalingam B; Cuesta-Munoz A; Davis E A; Matschinsky F M; Harrison R W;

Weber I T
CS Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
SO Diabetes, (1999 Sep) 48 (9) 1698-705.
Journal code: 0372763. ISSN: 0012-1797.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199909
ED Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990930

L2 ANSWER 9 OF 9 MEDLINE on STN
AN 1999275795 MEDLINE
DN PubMed ID: 10348039
TI Glucolipsin A and B, two new **glucokinase activators** produced by Streptomyces purpurogeniscleroticus and Nocardia vaccinii.
AU Qian-Cutrone J; Ueki T; Huang S; Mookhtiar K A; Ezekiel R; Kalinowski S S; Brown K S; Golik J; Lowe S; Pirnik D M; Hugill R; Veitch J A; Klohr S E; Whitney J L; Manly S P
CS Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, Connecticut 06492, USA.
SO Journal of antibiotics, (1999 Mar) 52 (3) 245-55.
Journal code: 0151115. ISSN: 0021-8820.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
ED Entered STN: 19990712
Last Updated on STN: 19990712
Entered Medline: 19990623

=> D ABS 6-9

L2 ANSWER 6 OF 9 MEDLINE on STN
AB The hormones glucagon and insulin delicately regulate the concentration of blood glucose. When patients become resistant to the effects of insulin or produce too little of it to properly regulate glucose concentrations, then diabetes can result. Unfortunately, not all patients with insulin-resistant, type 2 diabetes mellitus respond to drugs that improve insulin sensitivity. However, there is reason to be hopeful. A new molecule that targets glucokinase (GK), the enzyme responsible for phosphorylating glucose in pancreatic beta cells and hepatic cells, acts to significantly reduce blood glucose concentrations in rodents. The GK activator RO-28-1675 increased the glucose affinity and Vmax of GK, and rats treated with RO-28-1675 had improved glucose tolerance and elevated glucose uptake in liver. These results provide the basis for improved drug design that may alleviate diabetes mellitus and the disorders that accompany it in patients.

L2 ANSWER 7 OF 9 MEDLINE on STN
AB In Type 2 diabetes, glucose homeostasis is impaired due to either a decrease in insulin secretion or insulin action. In this symposium, molecular targets that could have an impact on either or both of these defects were discussed and data related to specific compounds were presented. Protein tyrosine phosphatase 1B inhibitors that relieve the negative control on insulin action and are active in cell assays, dipeptidyl peptidase IV inhibitors that raise postprandial glucagon-like peptide 1 levels in animals and humans, and pyruvate dehydrogenase kinase

inhibitors that increase the levels of pyruvate dehydrogenase, which in turn improve insulin sensitivity, were all discussed. Roche presented for the first time their novel **glucokinase activators** and discussed both the in vitro and in vivo activity profiles of representative **glucokinase activators** as potential therapy for Type 2 diabetes. Second generation retinoid X receptor modulators that retain the desirable effects of full agonists, while devoid of their negative attributes, such as triglyceride accumulation, were discussed. Also, clinical efficacy results of synthetic exendin-4, Exenatide trade mark, a glucagon-like peptide 1 analogue, were presented. In the area of obesity, agonists of several central (melanocortin type 4, serotonin subtype 2C and cannabinoid receptor 1) receptors and one peripheral G-protein-coupled receptor, cholecystokinin receptor-A, all of which lead to reduced food intake in animals, were discussed.

L2 ANSWER 8 OF 9 MEDLINE on STN

AB Mutations in human glucokinase are implicated in the development of diabetes and hypoglycemia. Human glucokinase shares 54% identical amino acid residues with human brain hexokinase I. This similarity was used to model the structure of glucokinase by analogy to the crystal structure of brain hexokinase. Glucokinase was modeled with both its substrates, glucose and MgATP, to understand the effect of mutations. The glucose is predicted to form hydrogen bond interactions with the side chains of glucokinase residues Thr 168, Lys 169, Asn 204, Asp 205, Asn 231, and Glu 290, similar to those observed for brain hexokinase I. The magnesium ion is coordinated by the carboxylates of Asp 78 and Asp 205 and the gamma-phosphate of ATP. ATP is predicted to form hydrogen bond interactions with residues Gly 81, Thr 82, Asn 83, Arg 85, Lys 169, Thr 228, Lys 296, Thr 332, and Ser 336. Mutations of residues close to the predicted ATP binding site produced dramatic changes in the Km for ATP, the catalytic rate, and a loss of cooperativity, which confirmed our model. Mutations of residues in the glucose binding site dramatically reduced the catalytic activity, as did a mutation that was predicted to disrupt an alpha-helix. Other mutations located far from the active site gave smaller changes in kinetic parameters. In the absence of a crystal structure for glucokinase, our models help rationalize the potential effects of mutations in diabetes and hypoglycemia, and the models may also facilitate the discovery of pharmacological **glucokinase activators** and inhibitors.

L2 ANSWER 9 OF 9 MEDLINE on STN

AB During the screening of the natural products for their ability to increase the activity of glucokinase by relieving inhibition by long chain fatty acyl CoA esters (FAC), two novel compounds, glucolipsin A (1) and B (2) were isolated from the butanol extracts of Streptomyces purpurogeniscleroticus WC71634 and Nocardia vaccinii WC65712, respectively. The structures of these two compounds were established by spectroscopic methods and chemical degradation. Glucolipsin A (1) and B (2) relieved the inhibition of glucokinase by FAC with RC50 values of 5.4 and 4.6 microM.

```
=> S GLUCOKINASE AND REVIEW AND (CLINICAL OR THERAPY) AND (2002/PY OR 2003/PY)
          2481 GLUCOKINASE
            31 GLUCOKINASES
          2483 GLUCOKINASE
                 (GLUCOKINASE OR GLUCOKINASES)
        400777 REVIEW
         50074 REVIEWS
        439842 REVIEW
                 (REVIEW OR REVIEWS)
       1358743 CLINICAL
            39 CLINICALS
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       1358767 CLINICAL
                 (CLINICAL OR CLINICALS)
       2333887 THERAPY
         58933 THERAPIES
       2354465 THERAPY
                 (THERAPY OR THERAPIES)
        539523 2002/PY
        566712 2003/PY
L3           2 GLUCOKINASE AND REVIEW AND (CLINICAL OR THERAPY) AND (2002/PY
               OR 2003/PY)

=> D 1-2

L3   ANSWER 1 OF 2     MEDLINE on STN
AN   2002331409     MEDLINE
DN   PubMed ID: 12073419
TI   Early-onset type 2 diabetes in Mexico.
AU   Garcia-Garcia Eduardo; Aguilar-Salinas Carlos A; Tusie-Luna Teresa;
     Rull-Rodrigo Juan Antonio
CS   Department of Endocrinology, and Metabolism, National Institute of Medical
     Sciences and Nutrition Salvador Zubiran, Mexico City, Mexico.
SO   Israel Medical Association journal : IMAJ, (2002 Jun) 4 (6)
     444-8.  Ref: 22
     Journal code: 100930740. ISSN: 1565-1088.
CY   Israel
DT   Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, TUTORIAL)
LA   English
FS   Priority Journals
EM   200207
ED   Entered STN: 20020621
     Last Updated on STN: 20020712
     Entered Medline: 20020711

L3   ANSWER 2 OF 2     MEDLINE on STN
AN   2002081828     MEDLINE
DN   PubMed ID: 11808879
TI   Heterogeneity of persistent hyperinsulinaemic hypoglycaemia. A series of
     175 cases.
AU   de Lonlay Pascale; Fournet Jean-Christophe; Touati Guy; Groos
     Marie-Sylvie; Martin Delphine; Sevin Caroline; Delagne Veronique; Mayaud
     Christine; Chigot Valerie; Sempoux Christine; Brusset Marie-Claire;
     Laborde Kathleen; Bellane-Chantelot Christine; Vassault Anne; Rahier
     Jacques; Junien Claudine; Brunelle Francis; Nihoul-Fekete Claire;
     Saudubray Jean-Marie; Robert Jean-Jacques
CS   Federation de Pediatrie, Hopital Necker-Enfants-Malades, Paris, France..
     pascale.de-lonlay@necker.fr
SO   European journal of pediatrics, (2002 Jan) 161 (1) 37-48.  Ref:
     27
     Journal code: 7603873. ISSN: 0340-6199.
CY   Germany: Germany, Federal Republic of
DT   Journal; Article; (JOURNAL ARTICLE)
     General Review; (REVIEW)
     (REVIEW, MULTICASE)
LA   English
FS   Priority Journals
EM   200204
ED   Entered STN: 20020128
     Last Updated on STN: 20021008
     Entered Medline: 20020410
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=> S HEXOKINASE ACTIVATORS
          7228 HEXOKINASE
           288 HEXOKINASES
          7261 HEXOKINASE
                 (HEXOKINASE OR HEXOKINASES)
         47366 ACTIVATORS
L4           0 HEXOKINASE ACTIVATORS
                 (HEXOKINASE(W)ACTIVATORS)

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